

I. AMENDMENTS TO THE CLAIMS

Claim 1. (Currently Amended) A compound of formula (I) or a salt thereof



(I)

wherein:

M-T is the residue of M-TH or M-TOH,

wherein M-TH and M-TOH are COX-2 selective inhibitors selected from the group consisting of: 4-(5-methyl-3-phenylisoxazol-4-yl)benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide, 4-(4-cyclohexyl-2-methyloxazol-5-yl)-2-fluorobenzenesulfonamide, N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1-oxo-1H-inden-5-yl]-methanesulfonamide, N-(4-nitro-2-phenoxyphenyl) methanesulfonanilide, N-(4-nitro-2-cyclohexyloxyphenyl)methane sulfonanilide, 2-[(2-chloro-6-fluorophenyl)amino]-5-methylbenzeneacetic acid, 2-[(2-chloro-6-fluorophenyl)-amino]-4-methylbenzeneacetic acid, and (Z)-2-(4-methylsulphonylphenyl)-3-phenyl-2-buten-1,4-diol,

wherein T = -SO₂NH-, -SO₂NR-, -CO-, -O-, -S-, -NH-, -N(SO₂R)-, R being an alkyl with 1-10 carbon atoms, and

~~wherein the COX-1 inhibiting activity/COX-2 inhibiting activity ratio (IC₅₀) of the COX-2 selective inhibitor, M-TH or M-TOH, is greater than or equal to 5,~~

$\text{Y}_A = \text{-(B)}_{b0}\text{-(T}_C\text{-Y)}_{c0}\text{-}$ wherein:

b0 and c0 are the integers 1 or 0, with the proviso that b0 and c0 cannot be simultaneously 0,

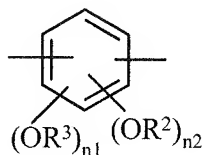
$\text{B} = \text{-T}_B\text{-X}_2\text{-T}_{B1}\text{-}$, in which:

$\text{T}_B = \text{CO or X}$, wherein X = O, S, NH, NR, and R is as defined above, T_B is CO when T is -SO₂NH-, -SO₂NR-, -O-, -S-, -NH-, or -N(SO₂R)-; and T_B is X when T is -CO-;

$\text{T}_{B1} = \text{CO or X}$, in which X is as defined above;

X₂ is a divalent radical and is selected from the following compounds:

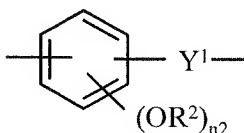
a)



wherein:

n₁ and n₂ are integers 0 or 1; R² and R³ are independently selected from H or CH₃;

b)

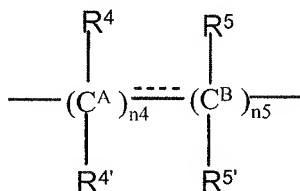


wherein:

n₂ and R² are as above defined;

Y¹ is -CH₂-CH₂- or -CH=CH-(CH₂)_{n2'}- wherein n_{2'} is an integer 0 or 1;

c)



wherein:

n₄ is an integer from 1 to 20 and n₅ is an integer from 0 to 20; R⁴, R^{4'}, R⁵ and R^{5'} are independently selected from the group consisting of _H, CH₃, OH, NH₂, NHCOCH₃, and _COOH; when the bond between the C^A and C^B carbons is a double bond, then R⁴ and R⁵ or R^{4'} and R^{5'} are absent;

T_C = CO, X wherein X is as defined above, or -(CH₂)_{n6}OC(O)- wherein n₆ is an integer from 1 to 20;

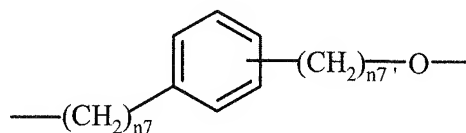
Y is a bivalent radical having the following meanings:

d) -R¹O-, in which R¹ is:

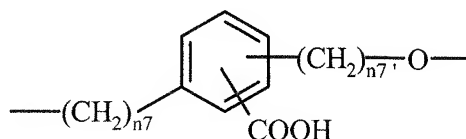
- straight or branched C₁-C₂₀-alkylene optionally containing one or more heteroatoms selected from oxygen, nitrogen, sulphur, or one or more groups -O(CO)-, -NH(CO)-,

-S(CO)-, optionally substituted with one or more of the following groups -OH, -SH, -NH₂, -NHCOR⁶, in which R⁶ is straight or branched C₁-C₁₀-alkyl;
- cycloalkylene containing from 5 to 7 carbon atoms into cycloalkylene ring, wherein one or more carbon atoms can be replaced by heteroatoms selected from nitrogen, oxygen or sulphur, and the ring can be substituted with side chains R⁶, R⁶ being as defined above;

e)

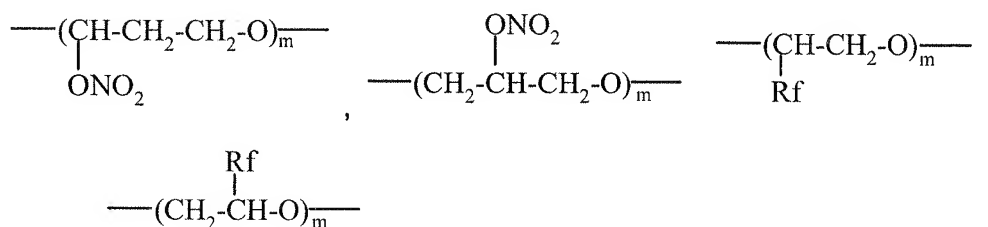


f)



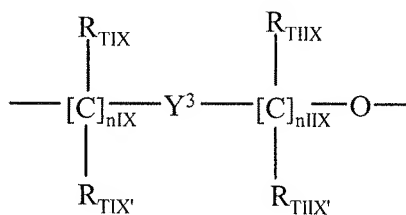
wherein $n7$ is an integer from 0 to 20, and $n7'$ is an integer from 1 to 20;

g)



wherein m is an integer from 1 to 6, Rf is a hydrogen atom or CH_3 ;

h)



(IA)

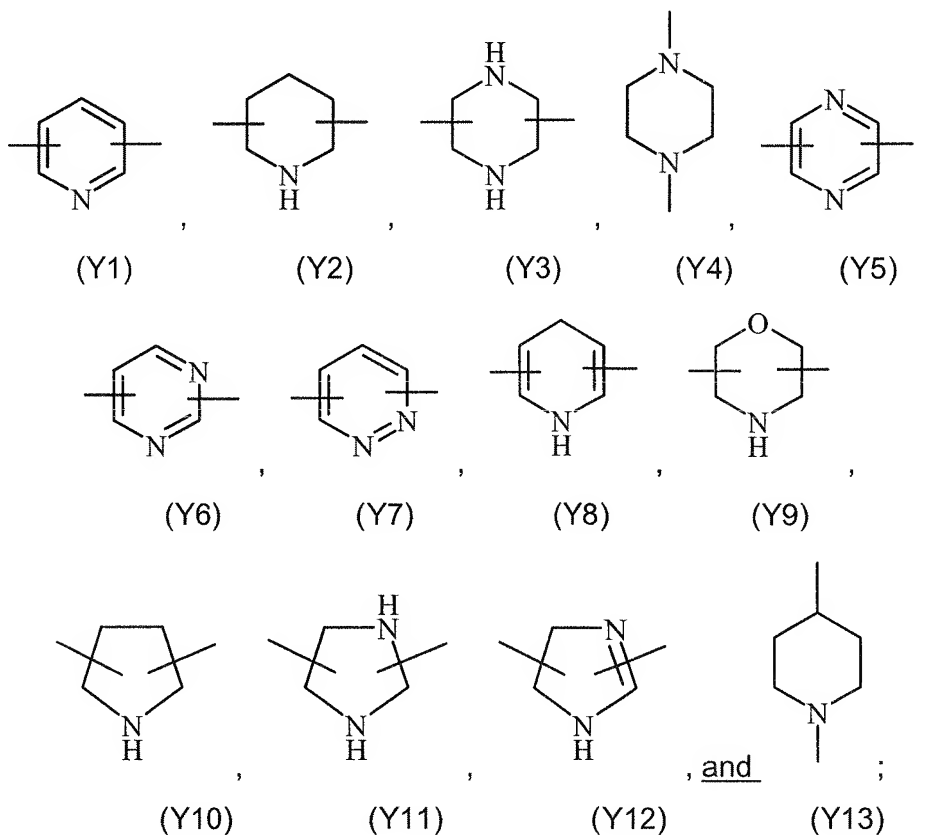
wherein:

n_{IX} is an integer from 0 to 10;

n_{IIX} is an integer from 1 to 10;

R_{TIX} , $R_{TIX'}$, R_{TIIX} , $R_{TIIX'}$, are the same or different, and are H or straight or branched C_1 - C_4 -alkyl;

Y^3 is ~~an heterocyclic saturated, unsaturated or aromatic 5 or 6 members ring,~~
containing one or more heteroatoms selected from nitrogen, oxygen, sulphur, and
selected from the group consisting of:



with the proviso that:

when $b_0 = 0$, $c_0 = 1$ and $T = -SO_2NH-$, $-SO_2NR-$, $-O-$, $-S-$, $-NH-$, $-N(SO_2R)-$ wherein R is as defined above, then $T_C = (CO)$ or $-(CH_2)_{n_6}O(CO)-$;

when $b_0 = 0$, $c_0 = 1$ and $T = CO$ then $T_C = X$ wherein X is as defined above;

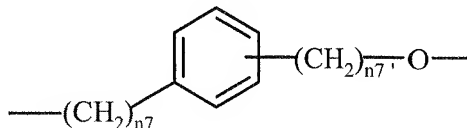
when $b_0 = 1$ and $T = -SO_2NH-$, $-SO_2NR-$, $-O-$, $-S-$, $-NH-$, $-N(SO_2R)-$ wherein R is as defined above, then $T_B = CO$;

when $b_0 = 1$ and $T = CO$ then $T_B = X$ wherein X is as defined above;

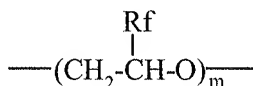
when $b_0 = 1$, $c_0 = 1$ and $T_{B1} = CO$ then $T_C = X$ wherein X is as above defined;

when $b_0 = 1$, $c_0 = 1$ and $T_{B1} = X$, wherein X is as above defined, then $T_C = (CO)$;
when $b_0 = 1$, $c_0 = 0$ the T_{B1} has only the meaning of $-O-$.

Claim 2. (Original) A compound of formula (I) according to claim 1 wherein $b_0 = 0$, $c_0 = 1$, T and T_C are as defined in claim 1, Y is a straight C_1 - C_6 alkylene or



wherein n_7 is 0 or 1, and $n_{7'}$ is 1 or 2, or



wherein m is 2, R_f is hydrogen.

Claim 3. (Original) A compound of formula (I) according to claim 2 wherein $b_0 = 0$, $c_0 = 1$, $T = -N(SO_2R)-$, $T_C = CO$ or $-(CH_2)_{n_6}O(CO)-$ wherein $n_6 = 1$ and $R = CH_3$.

Claim 4. (Previously Presented) A compound of formula (I) according to claim 2 wherein $b_0 = 0$, $c_0 = 1$, $T = -SO_2NH-$ and $T_C = CO$ or $-(CH_2)_{n_6}O(CO)-$ wherein $n_6 = 1$.

Claim 5. (Canceled)

Claim 6. (Original) A compound according to claim 3, that is N -[6-(2,4-difluorophenylthio)-2,3-dihydro-1-oxo-1-inden-5-yl]- N -[(4-nitrooxy)butyroxymethyl]methanesulfonamide.

Claim 7. (Original) A compound according to claim 3, that is N -[6-(2,4-difluorophenylthio)-2,3-dihydro-1-oxo-1-inden-5-yl]- N -[3-(nitrooxymethyl)benzoyloxymethyl]methanesulfonamide.

Claim 8. (Original) A compound according to claim 3, that is (Z) -2-(4-methylsulphonylphenyl)-3-phenyl-2-buten-1,4-diol-1-[(4-nitrooxymethyl)-benzoate]].

Claim 9. (Original) A compound according to claim 4, that is N-[4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenylsulfonyl]-4-nitrooxybutanamide.

Claim 10. (Original) A compound according to claim 3, that is N-(3-nitrooxymethyl)benzoyloxymethyl-N-(2-phenoxy-4-nitrophenyl)methane-sulfonamide.

Claim 11. (Previously Presented) A compound of formula (I) or a salt thereof according to claim 1, wherein said compound is a therapeutic agent.

Claim 12. (Previously Presented) A method of treatment or prophylaxis of inflammatory disorders, pain and fever, comprising administering to a subject a compound of formula (I) or a salt thereof according to claim 1.

Claim 13. (Previously Presented) A method according to claim 12, wherein the inflammatory disorders are selected from the group consisting of: arthritis, rheumatoid arthritis, osteoarthritis, dysmenhorrea, allergic rhinitis, sinusitis, chronic obstructive pulmonary diseases, dermatitis, psoriasis, cystic fibrosis, multiple sclerosis, vasculitis and organ transplant rejection.

Claim 14. (Previously Presented) A method of treatment or prophylaxis of cardiovascular diseases, comprising administering to a subject a compound of formula (I) or a salt thereof according to claim 1.

Claim 15. (Previously Presented) A method according to claim 14, wherein the cardiovascular diseases are selected from the group consisting of: atherosclerosis, restenosis, coronary artery disease, angina, diabetes mellitus, diabetic nephropathy, diabetic retinopathy, stroke and myocardic infarct.

Claim 16. (Previously Presented) A method of treatment or prophylaxis of gastrointestinal disorders, comprising administering to a subject a compound of formula (I) or a salt thereof according to claim 1.

Claim 17. (Previously Presented) A method according to claim 16 wherein the gastrointestinal disorders are selected from the group consisting of: inflammatory intestinal disorders, Crohn's disease, gastritis, ulcerative colitis, peptic ulcer, haemorrhagic ulcer, gastric hyperacidity, dyspepsia, gastroparesis, Zollinger-Ellison's syndrome, bacterial infections, hypersecretory states associated with systemic mastocytosis or basophilic leukaemia and hyperhystaminemia.

Claim 18. (Previously Presented) A method of treatment or prophylaxis of tumors and Alzheimer's disease, comprising administering to a subject a compound of formula (I) or a salt thereof according to claim 1.

Claim 19. (Previously Presented) A method of treating or preventing disorders resulting from elevated levels of COX-2, comprising administering to a subject a compound of formula (I) or a salt thereof according to claim 1.

Claim 20. (Previously Presented) A method according to claim 19, wherein the disorders resulting from elevated levels of COX-2 are selected from the group consisting of: angiogenesis, arthritis, asthma, bronchitis, menstrual cramps, tendinitis, bursitis, neoplasia, ophthalmic diseases, pulmonary inflammations, central nervous system disorders, allergic rhinitis, atherosclerosis, endothelial disorders, organs and tissues preservation, and inhibition or prevention of platelet aggregation.

Claim 21. (Previously Presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a pharmaceutically effective amount of a compound of general formula (I) or a salt thereof according to claim 1.

Claim 22. (Original) A composition according to claim 21 in a suitable form for the oral, parenteral, rectal, topic and transdermic administration, by inhalation spray or aerosol or iontophoresis devices.

Claim 23. (Previously Presented) A liquid or solid pharmaceutical composition for oral, parenteral, rectal, topic and transdermic administration or inhalation in the form of tablets, capsules and pills optionally with enteric coating, powders, granules, gels,

emulsions, solutions, suspensions, syrups, elixir, injectable forms, suppositories, in transdermal patches or liposomes, containing a compound of formula (I) according to claim 1 or a salt thereof and a pharmaceutically acceptable carrier.